1: Z Kardiol 1996 Jul;85(7):509-18

[Incidence and localization of apoptosis bodies in human arteriosclerosis lesions]

[Article in German]

Bauriedel G, Schluckebier S, Welsch U, Klingel K, Kandolf R, Steinbeck G.

Medizinische Klinik I, Klinikum Grosshadern, Ludwig-Maximilians-Universitat, Munchen.

Increased density of smooth muscle cells is an accepted feature of human restenosis after angioplasty. In addition to migration and proliferation, deregulated forms of programmed cell death may represent pathogenic mechanisms which lead to increased intimal cellularity. The goal of the present study was (i) to demonstrate programmed cell death in human plaque tissue by the detection of apoptotic bodies and to distinguish it from cellular necrosis, (ii) to evaluate the frequency and the localization of apoptotic bodies, and (iii) to compare restenotic and primary lesions for different expression patterns. To this end, coronary and peripheral atherectomy specimens from 14 restenotic and 25 primary lesions were examined by electron microscopy and morphometric analysis. Apoptotic bodies were distinguished from cellular necroses due to distinct morphological features, and were observed extracellularly, isolated or cell membrane-bound, as well as intracellularly in smooth muscle cells and macrophages. The main finding of this study is that hypercellular restenotic tissue from both coronary and peripheral lesions contains fewer apoptotic bodies than hypocellular plaques from primary lesions ($p < 0.01$ and $p < 0.05$, respectively). Most importantly, a highly significant, inverse correlation was seen between the density of apoptotic bodies and intimal cellularity ($r = -0.67$; $p < 0.0001$). Especially in the extracellular matrix regions, restenotic lesions showed fewer apoptotic bodies ($p < 0.001$). Again, these plaques exhibited a smaller number of apoptotic bodies with intracellular or membrane-bound localization; however, this observation was without statistical significance compared to primary lesions. For both plaque types, apoptotic bodies were found more frequently (by the factor 4-10) in the presence of smooth muscle cells than with macrophages. With respect to the cellular composition of the plaques, apoptotic bodies were

evenly detected in 15-28% of all smooth muscle cells and macrophages. Our results document a considerable intimal density of apoptotic bodies in high-grade human arteriosclerotic lesions and, in addition, reveal nearby smooth muscle cells and macrophages exhibiting intensive phagocytotic capacity. Differences in the density of apoptotic bodies and in cellularity, coincident with an inverse correlation between these determinants, were observed for restenotic and primary tissue. These findings strongly point to deregulated forms of programmed cell death as important pathogenic mechanisms involved in human restenosis.

PMID: 8928549 [PubMed - indexed for MEDLINE]

1: J Pathol 2000 Feb;190(3):267-80

The role of apoptosis in vascular disease.

Kockx MM, Knaapen MW.

Department of Pathology, A.Z. Middelheim, Antwerp, Belgium.
mark.kockx@uia.ua.ac.be

Normal arteries are characterized by a low turnover of endothelial (EC) and smooth muscle cells (SMC). Different mechanisms protect the EC and SMC against apoptosis in the normal artery. In hypertension, SMC replication is increased but this is not counterbalanced by increased apoptosis, resulting in thickening of the media of arteries and arterioles. The significance of apoptosis in atherosclerosis depends on the stage of the plaque, localization and the cell types involved. Both macrophages and SMC undergo apoptosis in atherosclerotic plaques. Apoptosis of macrophages is mainly present in regions showing signs of DNA synthesis/repair. SMC apoptosis is mainly present in less cellular regions and is not associated with DNA synthesis/repair. Even in the early stages of atherosclerosis SMC become susceptible to apoptosis since they increase different pro-apoptotic factors. Moreover, recent data indicate that SMC may be killed by activated macrophages. The loss of the SMC can be detrimental for plaque stability since most of the interstitial collagen fibres, which are important for the tensile strength of the fibrous cap, are produced by SMC. Apoptosis of macrophages could be beneficial for plaque stability if apoptotic bodies were removed. Apoptotic cells that are not scavenged in the plaque activate thrombin, which could further induce intraplaque thrombosis. It can be concluded that apoptosis in primary atherosclerosis is detrimental since it could lead to plaque rupture and thrombosis. Recent data of our group indicate that apoptosis decreased after lipid lowering which could be important in the understanding of the cell biology of plaque stabilization. Copyright 2000 John Wiley & Sons, Ltd.

Publication Types:
- Review
- Review, Tutorial

PMID: 10685061 [PubMed - indexed for MEDLINE]

1: Cardiovasc Res 2000 Feb;45(3):736-46 Related Articles, NEW Books, LinkOut

ELSEVIER SCIENCE FULL-TEXT ARTICLE

Apoptosis in atherosclerosis: beneficial or detrimental?

Kockx MM, Herman AG.

Department of Pathology, A.Z. Middelheim, Antwerp, Belgium. mark.kockx@uia.ua.ac.be

Several groups have demonstrated apoptotic cell death in atherosclerotic plaques. The significance of apoptosis in atherosclerosis depends on the stage of the plaque, localization and the cell types involved. Both macrophages and smooth muscle cells undergo apoptosis in atherosclerotic plaques. Apoptosis of macrophages is mainly present in regions showing signs of DNA synthesis/repair. Smooth muscle cell apoptosis is mainly present in less cellular regions and is not associated with DNA synthesis/repair. Even in early stages of atherosclerosis smooth muscle cells become susceptible to undergoing apoptosis since they increase different pro-apoptotic factors. Moreover, recent data indicate that smooth muscle cells may be killed by activated macrophages. The loss of the smooth muscle cells can be detrimental for plaque stability since most of the interstitial collagen fibers, which are important for the tensile strength of the fibrous cap, are produced by SMC. Apoptosis of macrophages could be beneficial for plaque stability if apoptotic bodies are removed. Apoptotic cells that are not scavenged in the plaque activate thrombin which could further induce intraplaque thrombosis. It can be concluded that apoptosis in the primary atherosclerosis is detrimental since it could lead to plaque rupture and thrombosis. Recent data of our group indicate that apoptosis decreases after lipid lowering which could be important in our understanding of the cell biology of plaque stabilization.

Publication Types:
- Review
- Review, Tutorial

PMID: 10728396 [PubMed - indexed for MEDLINE]

1: Pathobiology 1999;67(5-6):306-10

Role of antigen-presenting cells in long-term antitumor response based on tumor-derived apoptotic body vaccination.

Henry F, Bretaudeau L, Hequet A, Barbieux I, Lieubeau B, Meflah K, Gregoire M.

Institut de biologie, INSERM U419, Nantes, France.

Cellular therapy prospects for cancer are based on the development of T cell response, resulting in efficient tumor rejection and long-term protection. We have previously shown that treatment combining injection of interleukin-2 and tumor-derived apoptotic bodies, but not tumor cell extracts, permits to reject parental tumor in 40% of rats. We observed the implication of antigen-presenting cells (APCs) and tumor-derived apoptotic bodies in the rejection of established peritoneal carcinomatosis. We demonstrated that apoptotic bodies could be efficiently phagocytosed by monocytes, triggering them to an APC phenotype. When using these phagocytosing APCs, derived from peritoneal or blood monocytes, the remission rate reached 80% of rats. However, due to the lack of specific markers of rat monocyte-derived cells, the precise role of APCs, dendritic cells and/or macrophages responsible for this therapeutic improvement remained to be clarified. In order to elucidate this question, we developed an in vivo preventive cellular therapy based on tumor-derived apoptotic bodies, where macrophages were either depleted or activated. We report here that in a preventive antitumoral apoptotic body vaccination that allows survival for 40% of treated rats, the antitumor response was characterized by a specific long-term memory (cured rats rejected a second parental tumor cell challenge). Depletion of resident macrophages with silica or clodronate liposomes appeared to promote apoptotic body vaccination efficiency, increasing the treatment to 66% of success. In this case, FACS analysis showed that peritoneal cells present are essentially immature APCs and freshly recruited NK cells. In contrast, the onset of peritoneal inflammation by thioglycollate, inducing massive recruitment and activation of macrophages, reduced the overall survival, whatever the treatment was. Also, even though the surviving rate was better in silica-treated rats than control, no long-term protection was elicited. Our data suggest that massive inflammation, recruiting numerous activated macrophages, could inhibit tumor antigen presentation by 'professional'

APCs having phagocytosed apoptotic bodies, and defavor a specific antitumoral T cell response. Although effective responses were developed against parental tumor cells with silica/apoptotic body treatment, they seemed only partial, limited to primary cytotoxic efficiency. In conclusion, even if macrophages did not appear necessary for a primary response to tumor cells, these cells seemed to be implicated in the establishment of memory and long-term antitumor response.

PMID: 10725809 [PubMed - indexed for MEDLINE]

=> d 1-3 all

L3 ANSWER 1 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001192892 EMBASE
TI [Atherosclerosis].
L'ATHEROSCLEROSE.
AU Bonnet J.
CS J. Bonnet, Insern U. 441, avenue du Haut Leveque, 33600 Pessac, France
SO Medecine/Sciences, (2001) 17/5 (559-567).
Refs: 64
ISSN: 0767-0974 CODEN: MSMSE4
CY France
DT Journal; General Review
FS 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LA French
SL English; French
AB Atherosclerosis is the most common cause of death in Western countries. Atherosclerosis can be considered as a chronic inflammation of the intimal part of large arteries. It results from an initial **endothelial dysfunction** due to several risk factors, leading to an accumulation of modified lipoproteins, monocyte-derived macrophages and T cells interacting with the normal cellular components of the arterial wall and inducing foam cell and necrotic core formation. In many cases, the development of these atherosclerotic plaques is limited by a fibrous cap surrounding the necrotic core and mainly composed of extra-cellular matrix proteins and smooth muscle cells. All these events lead to the development of atherosclerotic plaques, which can protrude into the arterial lumen and induce such clinical manifestation as angina pectoris. One of the main complications of the atherosclerosis is the plaque rupture leading to vessel occlusion and acute clinical syndromes such as myocardial infarction or stroke. The plaque rupture results mainly from the acute accumulation of macrophages leading to the local secretion of metalloproteinases, extracellular matrix degradation and smooth muscle cell apoptosis inducing significant thinning and rupture of the fibrous cap. The plaque rupture exposes lipids, **apoptotic bodies** and tissue factor accumulated in necrotic core to blood components, initiating the coagulation cascade, platelet activation and thrombosis. Considering this process as a whole, biologists and physicians have to prevent, detect and treat the atherosclerotic lesions at each step of their evolution: the isolated risk factors, the initial **endothelial dysfunction**, the chronic inflammatory process responsible of atherosclerotic progression and the plaque rupture and thrombosis.
CT Medical Descriptors:
*atherosclerosis
endothelium lesion
risk factor
foam cell
atherosclerotic plaque
smooth muscle fiber
angina pectoris
blood vessel occlusion
heart infarction
stroke
enzyme release
extracellular matrix
apoptosis
thrombocyte activation
thrombosis
disease association
immunohistology
review

Drug Descriptors:
lipoprotein
metalloproteinase
thromboplastin
scleroprotein
RN (metalloproteinase) 81669-70-7; (thromboplastin) 9035-58-9

L3 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:369208 BIOSIS
DN PREV200100369208
TI Atherosclerosis.
Original Title: L'atherosclerose..
AU Bonnet, Jacques (1)
CS (1) Inserm U. 441, avenue du Hau-Leveque, 33600, Pessac France
SO M-S (Medecine Sciences), (Mai, 2001) Vol. 17, No. 5, pp. 559-567. print.
ISSN: 0767-0974.
DT General Review
LA French
SL English; French
AB Atherosclerosis is the most common cause of death in Western countries. Atherosclerosis can be considered as a chronic inflammation of the intimal part of large arteries. It results from an initial **endothelial dysfunction** due to several risk factors, leading to an accumulation of modified lipoproteins, monocyte-derived macrophages and T cells interacting with the normal cellular components of the arterial wall and inducing foam cell and necrotic core formation. In many cases, the development of these atherosclerotic plaques is limited by a fibrous cap surrounding the necrotic core and mainly composed of extracellular matrix proteins and smooth muscle cells. All these events lead to the development of atherosclerotic plaques, which can protrude into the arterial lumen and induce such clinical manifestation as angina pectoris. One of the main complications of the atherosclerosis is the plaque rupture leading to vessel occlusion and acute clinical syndromes such as myocardial infarction or stroke. The plaque rupture results mainly from the acute accumulation of macrophages leading to the local secretion of metalloproteinases, extracellular matrix degradation and smooth muscle cell apoptosis inducing significant thinning and rupture of the fibrous cap. The plaque rupture exposes lipids, **apoptotic bodies** and tissue factor accumulated in necrotic core to blood components, initiating the coagulation cascade, platelet activation and thrombosis. Considering this process as a whole, biologists and physicians have to prevent, detect and treat the atherosclerotic lesions at each step of their evolution: the isolated risk factors, the initial **endothelial dysfunction**, the chronic inflammatory process responsible of atherosclerotic progression and the plaque rupture and thrombosis.
CC Cytology and Cytochemistry - General *02502
Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Cardiovascular System - Physiology and Biochemistry *14504
Cardiovascular System - Heart Pathology *14506
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Muscle - Physiology and Biochemistry *17504
Immunology and Immunochemistry - General; Methods *34502
BC Animalia - Unspecified 33000
IT Major Concepts
Cell Biology; Cardiovascular System (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
T cells: blood and lymphatics, immune system; arterial wall: circulatory system; endothelium: circulatory system, dysfunction;

extracellular matrix: degradation; large arteries: circulatory system, inflammation; monocyte-derived macrophages: accumulation, blood and lymphatics, immune system; platelet: activation, blood and lymphatics; smooth muscle cells: muscular system

IT Diseases
angina pectoris: heart disease, vascular disease; atherosclerosis: vascular disease; **endothelial dysfunction**: vascular disease; myocardial infarction: heart disease, vascular disease; vessel occlusion: vascular disease

IT Chemicals & Biochemicals
extracellular matrix proteins; lipoproteins; metalloproteinases: secretion

IT Alternate Indexing
Angina Pectoris (MeSH); Atherosclerosis (MeSH); Myocardial Infarction (MeSH)

IT Miscellaneous Descriptors
apoptosis; coagulation cascade; disease development; disease progression; inflammatory process; necrosis; risk factors; thrombosis

ORGN Super Taxa
Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
animal (Animalia); human (Hominidae): patient

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 81669-70-7 (METALLOPROTEINASES)

L3 ANSWER 3 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R)

AN 2001:454827 SCISEARCH

GA The Genuine Article (R) Number: 436PU

TI Atherosclerosis

AU Bonnet J (Reprint)

CS Inserm U441, Ave Haut Leveque, F-33600 Pessac, France (Reprint); Inserm U441, F-33600 Pessac, France

CYA France

SO M S-MEDECINE SCIENCES, (MAY 2001) Vol. 17, No. 5, pp. 559-567.
Publisher: MASSON EDITEUR, 120 BLVD SAINT-GERMAIN, 75280 PARIS 06, FRANCE.
ISSN: 0767-0974.

DT Article; Journal

LA French

REC Reference Count: 64

AB Atherosclerosis is the most common cause of death in western countries; Atherosclerosis can be considered as a chronic inflammation of the intimal part of large arteries. It results from an initial **endothelial dysfunction** clue to several risk factors, leading to an accumulation of modified lipoproteins, monocyte-derived macrophages and T cells interacting with the normal cellular components of the arterial wall and inducing foam cell and necrotic core formation. In many cases, the development of these atherosclerotic plaques is limited by a fibrous cap surrounding the necrotic core and mainly composed of extra-cellular matrix;proteins and smooth muscle cells. All these events lead to the development of atherosclerotic plaques, which can protrude into :the arterial lumen and induce such clinical manifestation as angina pectoris. One of the main complications of the atherosclerosis is the plaque rupture leading to vessel occlusion and acute clinical syndromes such as myocardial infarction or stroke. The plaque rupture results mainly from the acute accumulation of macrophages leading:to the: local secretion of metalloproteinases, extracellular matrix degradation and smooth muscle cell apoptosis inducing significant thinning and rupture of the fibrous cap. The plaque rupture expose lipids, **apoptotic bodies** and tissue factor accumulated in necrotic core to blood components, initiating the coagulation cascade, platelet activation and thrombosis. Considering this process as a whole, biologists and physicians have to prevent, detect and treat the atherosclerotic lesions at each step of their evolution: the isolated risk factors, the initial

endothelial dysfunction, the chronic inflammatory process responsible of atherosclerotic progression and the plaque rupture and thrombosis.

CC MEDICINE, RESEARCH & EXPERIMENTAL

STP KeyWords Plus (R): SMOOTH-MUSCLE CELLS; CHLAMYDIA-PNEUMONIAE INFECTION; AMERICAN-HEART-ASSOCIATION; CORONARY-ARTERY DISEASE; INTIMA-MEDIA THICKNESS; RAT CAROTID-ARTERY; GROWTH-FACTOR-BETA; **ENDOTHELIAL DYSFUNCTION**; VASCULAR CELL; FAMILIAL HYPERCHOLESTEROLEMIA

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
AGGOUN Y	2000	20	2070	ARTERIOSCL THROM VAS
AIELLO R J	1999	19	1518	ARTERIOSCL THROM VAS
AIKAWA M	1995	2	14	J ATHEROSCLER THROMB
AKIMOTO S	2000	86	185	CIRC RES
ALLAN P L	1997	28	348	STROKE
ALLEN S	1998	13	439	CURR OPIN CARDIOL
ANDERSON J L	1999	99	1540	CIRCULATION
BAKKER S J L	2000	148	17	ATHEROSCLEROSIS
BANDOH T	2000	35	136	J CARDIOVASC PHARM
BECKER C R	2000	10	629	EUR RADIOL
BELLOSTA S	2000	23	B72	DIABETES CARE S2
BENDITT E P	1973	70	1753	P NATL ACAD SCI USA
BOISVERT W	1998	101	2702	J CLIN INVEST
BOQUIST S	1999	100	723	CIRCULATION
CARR A C	2000	87	349	CIRC RES
CHANNON K M	2000	20	1873	ARTERIOSCL THROM VAS
CLOWES A W	1985	56	139	CIRC RES
CRAWLEY J	2000	20	1362	ARTERIOSCL THROM VAS
DAVIES M J	1993	69	377	BRIT HEART J
DELERIVE P	2000	275	36703	J BIOL CHEM
DELEMOS J A	2000	36	423	J AM COLL CARDIOL
DONG Z M	2000	101	2290	CIRCULATION
DUFOURCQ P	1998	18	168	ARTERIOSCL THROM VAS
DUPLAA C	1996	121	253	ATHEROSCLEROSIS
EBERHARDT R T	2000	106	483	J CLIN INVEST
FALK E	1999	138	S421	AM HEART J S 2
FROSTEGARD J	1999	145	33	ATHEROSCLEROSIS
GLAGOV S	1987	316	1371	NEW ENGL J MED
GOODFELLOW J	2000	35	265	J AM COLL CARDIOL
GOSLING J	1999	103	773	J CLIN INVEST
GRAINGER D J	1998	111	2977	J CELL SCI 19
GUZIK T J	2000	86	E85	CIRC RES
JONASSON L	1986	6	131	ARTERIOSCLEROSIS
KATAOKA H	1999	99	3110	CIRCULATION
KIRK E A	2000	20	1529	ARTERIOSCL THROM VAS
KOCKX M M	2000	45	736	CARDIOVASC RES
LIUBA P	2000	102	1039	CIRCULATION
MACH F	1998	394	200	NATURE
MACH F	1997	94	1931	P NATL ACAD SCI USA
MALLAT Z	1999	85	E17	CIRC RES
MALLAT Z	1999	99	348	CIRCULATION
MASON D P	1999	85	1179	CIRC RES
MAYR M	2000	102	833	CIRCULATION
MEMON R A	2000	20	1536	ARTERIOSCL THROM VAS
MORENO P R	1996	94	3098	CIRCULATION
MORLA A O	2000	272	298	BIOCHEM BIOPH RES CO
OBRIEN E R	1993	73	223	CIRC RES
OISHI Y	2000	11	77	CORONARY ARTERY DIS
OWENS G K	1998	164	623	ACTA PHYSIOL SCAND
PAIKER J E	2000	37	174	ANN CLIN BIOCHEM 2
PASTERKAMP G	2000	150	245	ATHEROSCLEROSIS
PRASAD A	2000	102	35	CIRCULATION

RAINES E W	2000	81	173	INT J EXP PATHOL
RESNICK N	2000	11	167	CURR OPIN LIPIDOL
ROSENFELD M E	2000	181	S492	J INFECT DIS S3
SABLOTZKI A	1997	11	763	EUR J CARDIO-THORAC
SALOMAA V	1999	353	1729	LANCET
SCHULTZ D	2000	20	1412	VASC BIOL
SHI W B	2000	86	1078	CIRC RES
STARY H C	1994	14	840	ARTERIOSCLER THROMB
STARY H C	1995	15	1512	ARTERIOSCL THROM VAS
TEDGUI A	2000	87	81	CIRC RES
TEPLYAKOV A I	2000	902	320	ANN NY ACAD SCI
TRUSKEY G A	1999	19	393	ARTERIOSCL THROM VAS

L6 ANSWER 21 OF 57 USPATFULL
AN 2001:233540 USPATFULL
TI Use of pro-apoptotic factors in treatment of atherosclerosis
IN Ferran, Christiane, West Roxbury, MA, United States
Arvelo, Maria B., Quincy, MA, United States
PI US 2001053769 A1 20011220
AI US 2001-765519 A1 20010119 (9)
PRAI US 2000-177535 20000121 (60)
DT Utility
FS APPLICATION
LN.CNT 1953
INCL INCLM: 514/044.000
INCLS: 424/093.210; 435/325.000
NCL NCLM: 514/044.000
NCLS: 424/093.210; 435/325.000
IC [7]
ICM: A61K048-00
ICS: C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 1 OF 57 CAPLUS COPYRIGHT 2002 ACS
AN 2001:863218 CAPLUS
TI Apoptotic entities for use in treatment of endothelium dysfunction disorders
IN Sauder, Daniel; Mandel, Arkady; Bolton, Anthony E.
PA Vasogen Ireland Limited, Ire.
SO PCT Int. Appl.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001089538	A2	20011129	WO 2001-CA760	20010525

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI CA 2000-2309417 A 20000525

L6 ANSWER 21 OF 57 USPATFULL
AN 2001:233540 USPATFULL
TI Use of pro-apoptotic factors in treatment of atherosclerosis
IN Ferran, Christiane, West Roxbury, MA, United States
Arvelo, Maria B., Quincy, MA, United States
PI US 2001053769 A1 20011220
AI US 2001-765519 A1 20010119 (9)
PRAI US 2000-177535 20000121 (60)
DT Utility
FS APPLICATION
LN.CNT 1953
INCL INCLM: 514/044.000
INCLS: 424/093.210; 435/325.000
NCL NCLM: 514/044.000
NCLS: 424/093.210; 435/325.000
IC [7]
ICM: A61K048-00
ICS: C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 1 OF 57 CAPLUS COPYRIGHT 2002 ACS
AN 2001:863218 CAPLUS
TI Apoptotic entities for use in treatment of endothelium dysfunction disorders
IN Sauder, Daniel; Mandel, Arkady; Bolton, Anthony E.
PA Vasogen Ireland Limited, Ire.
SO PCT Int. Appl.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001089538	A2	20011129	WO 2001-CA760	20010525

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI CA 2000-2309417 A 20000525

L5 ANSWER 53 OF 55 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 96:580230 SCISEARCH
GA The Genuine Article (R) Number: UZ426
TI FREQUENCY AND LOCALIZATION OF APOPTOTIC BODIES IN HUMAN ARTERIOSCLEROSIS - RESTENOTIC VERSUS PRIMARY CORONARY AND PERIPHERAL LESIONS AFTER PERCUTANEOUS ATHERECTOMY
AU BAURIEDEL G (Reprint); SCHLUCKEBIER S; WELSCH U; KLINGEL K; KANDOLF R; STEINBECK G
CS UNIV MUNICH, KLINIKUM GROSSHADERN, MED KLIN 1, MARCHIONINISTR 15, D-81377 MUNICH, GERMANY (Reprint); UNIV MUNICH, ANAT ANSTALT, D-81377 MUNICH, GERMANY; UNIV TUBINGEN, INST PATHOL, D-72076 TUBINGEN, GERMANY
CYA GERMANY
SO ZEITSCHRIFT FUR KARDIOLOGIE, (JUL 1996) Vol. 85, No. 7, pp. 509-518. ISSN: 0300-5860.
DT Article; Journal
FS LIFE; CLIN
LA German
REC Reference Count: 46
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L5 ANSWER 34 OF 55 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:480936 BIOSIS
DN PREV199699196192
TI Frequency and localization of apoptotic bodies in human arteriosclerosis. Restenotic versus primary coronary and peripheral lesions after percutaneous atherectomy.
AU Bauriedel, G. (1); Schluckebier, S.; Welsch, U.; Klingel, K.; Kandolf, R.; Steinbeck, G.
CS (1) Med. Klinik I, Klinikum Grosshadern, Ludwig-Maximilians-Univ., Machioninistrasse 15, 81377 Muenchen Germany
SO Zeitschrift fuer Kardiologie, (1996) Vol. 85, No. 7, pp. 509-518. ISSN: 0300-5860.
DT Article
LA German
SL German; English

L5 ANSWER 2 OF 55 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 2001050998 EMBASE
TI Adventitial infiltrates associated with advanced atherosclerotic plaques: Structural organization suggests generation of local humoral immune responses.
AU Houtkamp M.A.; de Boer O.J.; van der Loos C.M.; van der Wal A.C.; Becker A.E.
CS Dr. A.E. Becker, Dept. of Cardiovascular Pathology, Academic Medical Center, University of Amsterdam, P.O. Box 22700, 1100 DE Amsterdam, Netherlands. m.i.schenker@amc.uva.nl
SO Journal of Pathology, (2001) 193/2 (263-269).
Refs: 42
ISSN: 0022-3417 CODEN: JPTLAS
CY United Kingdom
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
LA English
SL English

L6 ANSWER 19 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 1998:912362 SCISEARCH
GA The Genuine Article (R) Number: 141XG
TI Cellular vaccines
AU Bartholeyns J (Reprint); RometLemonne J L; Chokri M; Buyse M; Velu T; Bruyns C; VandeWinkel J J; Heeney J; Koopman G; Malmsten M; DeGroote D; Monsigny M; Midoux P; Alarcon B
CS IDM, PARIS, FRANCE (Reprint); ID2, BRUSSELS, BELGIUM; ULB, BRUSSELS, BELGIUM; UNIV UTRECHT HOSP, UTRECHT, NETHERLANDS; BPRC RIJSWIJK, RIJSWIJK, NETHERLANDS; YKI, STOCKHOLM, SWEDEN; BIOSOURCE, NIVELLES, BELGIUM: CNRS. F-45071 ORLEANS, FRANCE; UNIV AUTONOMA MADRID CANTOBLANCO, CSIC, MADRID, SPAIN
CYA FRANCE; BELGIUM; NETHERLANDS; SWEDEN; SPAIN
SO RESEARCH IN IMMUNOLOGY, (SEP-OCT 1998) Vol. 149, No. 7-8, pp. 647-649.
Publisher: EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER, 23 RUE LINOIS, 75724 PARIS CEDEX 15, FRANCE.
ISSN: 0923-2494.
DT Article; Journal
FS LIFE

LA English
REC Reference Count: 0
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

File 411:DIALINDEX(R)

DIALINDEX(R)
(c) 2002 The Dialog Corporation plc

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
?sf medicine
You have 29 files in your file list.
(To see banners, use SHOW FILES command)
?s apopto?(w)bod?

Your SELECT statement is:
s apopto?(w)bod?

Items	File
1106	5: Biosis Previews(R)_1969-2002/Feb W1
2952	34: SciSearch(R) Cited Ref Sci_1990-2002/Feb W2
24	35: Dissertation Abs Online_1861-2002/Feb
1	48: SPORTDiscus_1962-2002/Feb
5	65: Inside Conferences_1993-2002/Feb W1
673	71: ELSEVIER BIOBASE_1994-2002/Feb W2
1007	73: EMBASE_1974-2002/Feb W1
4	77: Conference Papers Index_1973-2002/Jan
1	91: MANTIS(TM)_1880-2001/Oct
96	94: JICST-EPlus_1985-2002/Dec W5
33	98: General Sci Abs/Full-Text_1984-2001/Dec
11	135: NewsRx Weekly Reports_1995-2002/Feb W2
442	144: Pascal_1973-2002/Feb W2
56	149: TGG Health&Wellness DB(SM)_1976-2002/Feb W1
1136	155: MEDLINE(R)_1966-2002/Jan W4
259	156: ToxFile_1966-2001/Oct W3
655	159: Cancerlit_1975-2001/Oct
39	162: CAB HEALTH_1983-2001/Dec
16	172: EMBASE Alert_2002/Feb W2
31	266: FEDRIP_2002/Dec
8	370: Science_1996-1999/Jul W3
55	399: CA SEARCH(R)_1967-2002/UD=13607
12	434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
26	442: AMA Journals_1982-2002/Mar B1
4	444: New England Journal of Med._1985-2002/Feb W2
9	457: The Lancet_1986-2000/Oct W1
3	467: ExtraMED(tm)_2000/Dec

27 files have one or more items; file list includes 29 files.

?b 34, 155
12feb02 10:14:11 User264783 Session D33.4
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$0.95 Estimated cost File411
$0.13 TYMNET
$1.08 Estimated cost this search
$3.30 Estimated total session cost 1.867 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 34:SciSearch(R) Cited Ref Sci 1990-2002/Feb W2
(c) 2002 Inst for Sci Info
File 155:MEDLINE(R) 1966-2002/Jan W4

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823560 BOD?
S1 4088 APOPTO?(W)BOD?
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2872561 PY=>2000
S2 3478 S1 NOT PY=>2000
?s s2 and (autoimmun? or inflamma?)
3478 S2
107779 AUTOIMMUN?
370121 INFLAMMA?
S3 398 S2 AND (AUTOIMMUN? OR INFLAMMA?)
?s s3 and (treat? or prophylaxis)
398 S3
2648430 TREAT?
63574 PROPHYLAXIS
S4 91 S3 AND (TREAT? OR PROPHYLAXIS)
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...examined 50 records (50)
...completed examining records
S5 81 RD (unique items) 5/9/1 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

08521535 Genuine Article#: 296FV Number of References: 9
Title: Role of antigen-presenting cells in long-term antitumor response
based on tumor-derived apoptotic body vaccination
Author(s): Henry F; Bretaudeau L; Hequet A; Barbieux I; Lieubeau B; Meflah

K; Gregoire M (REPRINT)
Corporate Source: INST BIOL,INSERM U419/F-44035 NANTES//FRANCE/ (REPRINT);
INST BIOL,INSERM U419/F-44035 NANTES//FRANCE/
Journal: PATHOBIOLOGY, 1999, V67, N5-6, P306-310
ISSN: 1015-2008 Publication date: 19990000
Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND
Language: English Document Type: ARTICLE
Geographic Location: FRANCE
Subfile: CC LIFE--Current Contents, Life Sciences
Journal Subject Category: CELL BIOLOGY; PATHOLOGY
Abstract: Cellular therapy prospects for cancer are based on the development of T cell response, resulting in efficient tumor rejection and long-term protection. We have previously shown that treatment combining injection of interleukin-2 and tumor-derived apoptotic bodies , but not tumor cell extracts, permits to reject parental tumor in 40% of rats. We observed the implication of antigen-presenting cells (APCs) and tumor-derived apoptotic bodies in the rejection of established peritoneal carcinamatosis. We demonstrated that apoptotic bodies could be efficiently phagocytosed by monocytes, triggering them to an APC phenotype. When using these phagocytosing APCs, derived from peritoneal or blood monocytes, the remission Fate reached 80% of rats. However, due to the lack of specific markers of rat monocyte-derived cells, the precise role of APCs, dendritic cells and/or macrophages responsible for this therapeutic improvement remained to be clarified. In order to elucidate this question, we developed an in vivo preventive cellular therapy based on tumor-derived apoptotic bodies , where macrophages were either depleted or activated. We report here that in a preventive antitumoral apoptotic body vaccination that allows survival for 40% of treated rats, the antitumor response was characterized by a specific long-term memory (cured rats rejected a second parental tumor cell challenge). Depletion of resident macrophages with silica or clodronate liposomes appeared to promote apoptotic body vaccination efficiency, increasing the treatment to 66% of success, in this case, FAGS analysis showed that peritoneal cells present are essentially immature APCs and freshly recruited NK cells. In contrast, the onset of peritoneal inflammation by thioglycollate, inducing massive recruitment and activation of macrophages, reduced the overall survival, whatever the treatment was. Also, even though the surviving rate was better in silica- treated rats than control, no longterm protection was elicited. Our data suggest that massive inflammation , recruiting numerous activated macrophages, could inhibit tumor antigen presentation by 'professional' APCs having phagocytosed apoptotic bodies , and defavor a specific antitumoral T cell response. Although effective responses were

developed against parental tumor cells with silica/ apoptotic body treatment , they seemed only partial, limited to primary cytotoxic efficiency. In conclusion, even if macrophages did not appear necessary for a primary response to tumor cells, these cells seemed to be implicated in the establishment of memory and long-term antitumor response. Copyright (C) 2000 S. Karger AG, Basel.
Descriptors--Author Keywords: antigen-presenting cells ; apoptotic bodies ; cellular therapy ; cancer
Identifiers--KeyWord Plus(R): CANCER
Cited References:
ALBERT ML, 1998, V392, P86, NATURE
BELLONE M, 1997, V159, P5391, J IMMUNOL
BOISTEAU O, 1997, V2, P403, APOPTOSIS
HAGUE A, 1993, V55, P498, INT J CANCER
HENRY F, 1999, V59, P3329, CANCER RES
HENRY F, 1998, V149, P673, RES IMMUNOL
PERRIN P, 1994, V107, P1697, GASTROENTEROLOGY
RONCHETTI A, 1999, V163, P1230, J IMMUNOL
SAVILL J, 1998, V392, P442, NATURE
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5/8/67 (Item 67 from file: 34)
DIALOG(R)File 34:(c) 2002 Inst for Sci Info. All rts. reserv.

05461777 Genuine Article#: WA465 Number of References: 98
Title: ADVERSE AND BENEFICIAL IMMUNOLOGICAL EFFECTS OF PURINE NUCLEOSIDE
ANALOGS (Abstract Available)
Journal Subject Category: HEMATOLOGY
Descriptors--Author Keywords: PURINE ANALOGS ; IMMUNOLOGICAL ACTION
Identifiers--KeyWords Plus: CHRONIC LYMPHOCYTIC-LEUKEMIA;
ADENOSINE-DEAMINASE DEFICIENCY; AUTOIMMUNE HEMOLYTIC-ANEMIA; DNA
STRAND BREAKS; COMBINED IMMUNODEFICIENCY DISEASE; BONE-MARROW
TRANSPLANTATION; PROGRAMMED CELL-DEATH; DEOXYADENOSINE TOXICITY;
FLUDARABINE PHOSPHATE; DEOXYCYTIDINE KINASE
Research Fronts: 95-2384 002 (CHRONIC LYMPHOCYTIC-LEUKEMIA; INCREASED
PERIPHERAL-BLOOD NORMAL MYELOID PROGENITOR CELLS (CFU-GM); FLUDARABINE
PLUS ARA-C+G-CSF)
95-2455 002 (POLY(ADP-RIBOSE) POLYMERASE; ACUTELY DNA DAMAGED CELLS;
H2O2-INDUCED APOPTOSIS)

95-0204 001 (FAS LIGAND; T-CELL APOPTOSIS; TEMPERATURE-SENSITIVE MUTANT
INDUCE FAS/APO-1 EXPRESSION)
95-1076 001 (INTERNUCLEOSOMAL DNA FRAGMENTATION DURING DRUG-INDUCED
APOPTOSIS; PROGRAMMED CELL-DEATH; APOPTOTIC BODIES)
95-4426 001 (GLUCOCORTICOID-INDUCED APOPTOSIS; PROGRAMMED CELL-DEATH;
DEOXYRIBONUCLEASE INDUCTION IN APOPTOTIC CYTOTOXIC T-LYMPHOCYTES)

File 34:SciSearch(R) Cited Ref Sci 1990-2002/Feb W2
(c) 2002 Inst for Sci Info

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E2 1975 RF=95-1076
E3 1206 *RF=95-1076 001 (INTERNUCLEOSOMAL DNA FRAGMENTAT
E4 430 RF=95-1076 002 (INTERNUCLEOSOMAL DNA FRAGMENTAT
E5 183 RF=95-1076 003 (INTERNUCLEOSOMAL DNA FRAGMENTAT
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E8 25 RF=95-1076 006 (INTERNUCLEOSOMAL DNA FRAGMENTAT
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E10 8 RF=95-1076 008 (INTERNUCLEOSOMAL DNA FRAGMENTAT
E11 1 RF=95-1076 009 (INTERNUCLEOSOMAL DNA FRAGMENTAT
E12 5 RF=95-1077

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?s e3
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1206 S2
1036611 TREAT?
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372 S3
1953857 PY=>2000
S4 372 S3 NOT PY=>2000
?s s4 and (autoimmune or inflam?)

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        372 S4
      41007 AUTOIMMUNE
     159043 INFLAM?
   S5     48 S4 AND (AUTOIMMUNE OR INFLAM?)

File 34:SciSearch(R) Cited Ref Sci 1990-2002/Feb W2
     (c) 2002 Inst for Sci Info

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Ref  Items  Index-term
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E2    1975  RF=95-1076
E3    1206 *RF=95-1076 001  (INTERNUCLEOSOMAL DNA FRAGMENTAT
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S1      1010  MULTIPLE(W)SCLEROSIS AND CYTOKINE?
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S3 0 S2 AND APOP?(W)BOD?
S4 2 S2 AND (IL2 OR LI3 OR IL4 OR IL5)
S5 486 PSORIASIS AND CYTOKINE?
S6 262 S5 AND EXPRESS?
S7 81 S6 AND TREAT?
S8 1 S7 AND APOP?

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S1 7225 AUTOIMMUNE? AND MECHANISM?
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S4 890 S3 AND AUTOIMMUNE(W)DISEASE?

10972725 21080879 PMID: 11213261
Antigen-specific T cells in autoimmune diseases with a focus on multiple sclerosis and experimental allergic encephalomyelitis.
Xiao BG; Link H
Division of Neurology, Karolinska Institute, Huddinge University Hospital, Stockholm, Sweden. bao-guoxiao@cnsf.ki.se
Cellular and molecular life sciences (Switzerland) Oct 1 1999, 56 (1-2) p5-21, ISSN 1420-682X Journal Code: CLE
Languages: ENGLISH
Document type: Journal Article; Review; Review, Academic
Record type: Completed
Subfile: INDEX MEDICUS
Although the pathogenesis of autoimmune diseases remains poorly understood, the current view is that autoaggresive antigen-specific T cells play a central role in the cascade of events leading to most autoimmune diseases . A major event in the development of autoimmune diseases is the activation of antigen-specific T cells-how, when and where does this activation take place? This review addresses questions concerning the occurrence of unique autoantigens triggering autoimmune diseases , the factors influencing the balance between self-tolerance and autoaggresive immunity, and the mechanisms by which dendritic cells mediate immunity and tolerance to antigen-specific T cells. Knowledge of how antigen-specific T cells are activated is now being used to develop therapeutic approaches to control autoimmune diseases . We discuss tolerance to antigen-specific T cells and tolerance induction as treatment of T-cell-mediated autoimmune diseases . Therapeutic modalities have been established which selectively target the pathogenic T cells. leaving the remainder of the immune system intact. (134 Refs.)
Tags: Animal; Human
Descriptors: Autoimmune Diseases --immunology--IM; *Encephalomyelitis, Experimental Autoimmune --immunology--IM; *Multiple Sclerosis--immunology --IM; *T-Lymphocytes--immunology--IM; Autoimmune Diseases --therapy--TH; Autoimmunity; Dendritic Cells--physiology--PH; Down-Regulation (Physiology) ; Encephalomyelitis, Experimental Autoimmune --therapy--TH; Lymphocyte Transformation; Mice; Models, Biological; Mucous Membrane--immunology--IM; Multiple Sclerosis--therapy--TH; Receptors, Antigen, T-Cell--metabolism--ME ; Vaccines--immunology--IM
CAS Registry No.: 0 (Receptors, Antigen, T-Cell); 0 (Vaccines)
Record Date Created: 20010212
4/9/3
DIALOG(R)File 155:MEDLINE(R)

Inhibition of CD40 signaling pathway in antigen presenting cells by T suppressor cells.

Liu Z; Tugulea S; Cortesini R; Lederman S; Suciu-Foca N

Department of Pathology, College of Physicians & Surgeons of Columbia University, New York, NY 10032, USA.

Human immunology (UNITED STATES) Jul 1999, 60 (7) p568-74, ISSN 0198-8859 Journal Code: G9W

Contract/Grant No.: 5-RO1-A125210-12, PHS

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

Understanding the mechanism which underlies the induction of

immunologic tolerance is crucial to the development of strategies for treatment of autoimmune diseases and allograft rejection. Although the concept that T suppressor cells (Ts) downregulate the immune response has long been accepted, the existence of a distinct population of lymphocytes that mediates suppression has not been convincingly demonstrated. In previous studies, we have utilized human T cell lines (TCLs) to analyze the suppressive effects of CD8+CD28 T cells in allogeneic, peptide specific and xeno-specific responses. In each case, CD8+CD28- T cells inhibit proliferation of CD4+ T helper lymphocytes (Th) with cognate antigen specificity. These CD8+CD28- T cells display the critical functional characteristics of T suppressor cells. Similar to the induction of CD8+ cytotoxic T cells (Tc) by Th, this process depends on antigen presenting cells (APC) acting as a "bridge" between MHC-class I specific CD8+ and class II specific CD4+ T cells. A possible explanation of Ts-mediated suppression is their ability to modulate the function of APCs. The present studies show that CD8+CD28- Ts directly inhibit the CD40 signaling pathway of APC by a contact-dependent mechanism that renders bridging APCs incapable of inducing CD4+ Th activation. The effects of Ts on the functional state of APC supports the concept that the order in which Ts and Th cells interact with cognate APCs determines the functional outcome of immune responses.

Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *Antigen-Presenting Cells--immunology--IM; *Antigens, CD40 --immunology--IM; *CD8-Positive T-Lymphocytes--immunology--IM; *Signal Transduction; Antigens, CD28--immunology--IM; CD4-Positive T-Lymphocytes --immunology--IM; CD40 Ligand; Cell Division; Cell Line; Membrane Glycoproteins--biosynthesis--BI; Membrane Glycoproteins--immunology--IM

CAS Registry No.: 0 (Antigens, CD28); 0 (Antigens, CD40); 0 (Membrane Glycoproteins); 147205-72-9 (CD40 Ligand)

Record Date Created: 19991008